2570 (—H stretching), 1722 (carboxyl acyl), and 1645 (amide acyl) cm.$^{-1}$.

(B). **With One Mole of Sodium Hydroxide.**—Reaction and product isolation was as above except that 0.71 g. (5.00 mmoles) of succinamoyl azide and 25 ml. (5.00 mmoles) of 0.200 *N* sodium hydroxide were employed and that no acid was added prior to chromatography. Succinimide (4) (0.27 g., 54%), m.p. 121–124°, was eluted with 10% ethanol in carbon tetrachloride, as proved by mixture melting point and infrared spectral comparison with authentic succinimide, m.p. 123–125°.

(C). **With Hydrochloric Acid.**—A mixture of succinamoyl azide (1.19 g., 8.38 mmoles) and hydrochloric acid (40 ml., 0.200 *N*, 8.00 mmoles) was stirred at room temperature in a constant pressure gas-measuring apparatus for 23 hr., at the end of which time the evolution of gas (10.1 mmole, 60% of theory for two moles) was complete. Isolation was by chromatography as above, and β-alanine amide hydrochloride (6) (0.53 g., 51% on 2), m.p. 146–148°, was eluted with 50% methanol in carbon tetrachloride. A single crystallization from ethanol afforded pure 6 as white leaflets, m.p. 149–150° (lit.[11,12] m.p. 149°) which exhibited infrared absorption (potassium bromide pellet) at 3360, 3165, 3125, 3000, and 2945 (—H stretching) and 1669 (amide acyl) cm.$^{-1}$.

Thermal Decomposition of Succinamoyl Azide (2). (A). **Pure.**—When 2 (0.327 g., 2.30 mmoles) was warmed in a constant pressure gas-measuring apparatus, vigorous decomposition occurred at 72° and decomposition product was scattered throughout the apparatus. The increase in volume corresponded to 2.24 mmoles (98% of theory for one mole) of gas. A portion of the decomposition product which was recovered showed infrared absorption (potassium bromide pellet) at 3340 (s), 3160 (s), 3060 (m), 2860 (w), 1740 (s), 1685 (s), and 1650 (s) cm.$^{-1}$.

(B). **In 1,2-Dimethoxyethane.**—A solution of 2 (1.05 g.) in 1,2-dimethoxyethane (50 ml.) was heated under reflux until gas evolution ceased (*ca.* 10 min.). Solvent was immediately removed under reduced pressure and at room temperature to yield a semisolid material, presumed to be β-isocyanatopropionamide (3), which exhibited infrared absorption (potassium bromide pellet) at 3370 (s), 3160 (m), 2920 (w), 2270 (s), 1740 (m), and 1655 (s) cm.$^{-1}$. After three days this material had an infrared spectrum virtually identical with that of the decomposition product in (A).

When the decomposition of 2 (0.88 g., 6.2 mmoles) was carried out in 1,2-dimethoxyethane (100 ml.) as above, and the solution was permitted to remain at room temperature for 108 hr., there was obtained, after removal of solvent at reduced pressure, a white solid which had an infrared spectrum similar to that of the decomposition product in (A). From chromatography of this white solid on silicic acid–Celite (30 g., 1:1 mixture) there was obtained dihydrouracil (7) (0.15 g., 21%), eluted with 10% methanol in carbon tetrachloride, and identical by the criterion of infrared spectral comparison with authentic 7.[13] Authentic 7 had m.p. 276–278° (lit.[13] m.p. 272–275°) and exhibited absorption in the infrared (potassium bromide pellet) at 3220, 3070, and 2880 (—H stretching); 1740 (broad, acyl); and 1693 (sharp, acyl) cm.$^{-1}$.

(C). **In 1,2-Dimethoxyethane with Addition of Trimethylamine.**—A solution of 2 (1.59 g., 11.2 mmoles) in 1,2-dimethoxyethane (100 ml.) was decomposed as in B), the solution was cooled, and to it was added trimethylamine (7 g.). After 12 hr. at room temperature, during which time solid crystallized from solution, the total mixture was evaporated under reduced pressure to yield a white solid (1.33 g., 108% of theory for loss of nitrogen gas) which was chromatographed on silicic acid–Celite (60 g., 1:1 mixture). Dihydrouracil (7) (0.90 g., 71% on 2), m.p. 257–271°, was eluted with 40% methanol in carbon tetrachloride, and was identical, by the criteria of mixture melting point and infrared spectral comparison, with the authentic sample of 7 described in (B).

(D). **In 1,2-Dimethoxyethane with Addition to Hydrochloric Acid.**—A solution of 2 (1.08 g., 7.6 mmoles) in 1,2-dimethoxyethane (100 ml.) was decomposed as in (B), cooled, and stirred into iced hydrochloric acid (10.0 mmoles). Silicic acid–Celite (5 g., 1:1 mixture) was added to the solution and the mixture was evaporated under reduced pressure to yield a free-flowing powder which was chromatographed as in (C). Elution of the column with 50% methanol in carbon tetrachloride afforded β-alanine amide hydrochloride (6) (0.72 g., 76%), m.p. 148–149°, identical, by the criteria of mixture melting point and infrared spectral comparison with the sample of pure 6 described above.

Irradiative Decomposition of Succinamoyl Azide (2).—A slurry of 2 (1.00 g.) in methylene chloride (100 ml.) was stirred in an irradiation apparatus fitted with a reflux condenser and, internally, with a Hanovia 54 A 36 S high pressure mercury lamp. Irradiation, in a nitrogen atmosphere and under vigorous reflux, was continued for 14 hr., when a sample of the product showed no infrared absorption in the 2100–2300-cm.$^{-1}$ region. By evaporation of the reaction mixture, there was obtained a white solid which had an infrared spectrum identical with that of the thermal decomposition product described in (B) above.

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Synthesis of Analgesics with Benzomorphane Structure. A Possible Intermediate: 1-Methyl-2-benzyl-4-piperidol

U. M. TEOTINO[1]

Research Laboratories, Lepetit S.p.A., Milan, Italy

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In the course of investigations concerning the synthesis of analgesics of the benzomorphane series it became of interest to prepare the intermediate 1-methyl-2-benzyl-4-piperidol (VII).

The following method of synthesis gave excellent results. Phenylacetaldehyde was condensed with monoethyl malonate as described by Moureau[2] to give ethyl 4-phenyl-2-butenoate in 65% yield. This ester, by treatment with methylamine as described by Morsch[3] for the reaction between methylamine and crotonic acid, was converted into *N*-methyl-3-methylamino-4-phenylbutyramide (I), which was in turn hydrolized to the free acid II. II was esterified giving ethyl 3-methylamino-

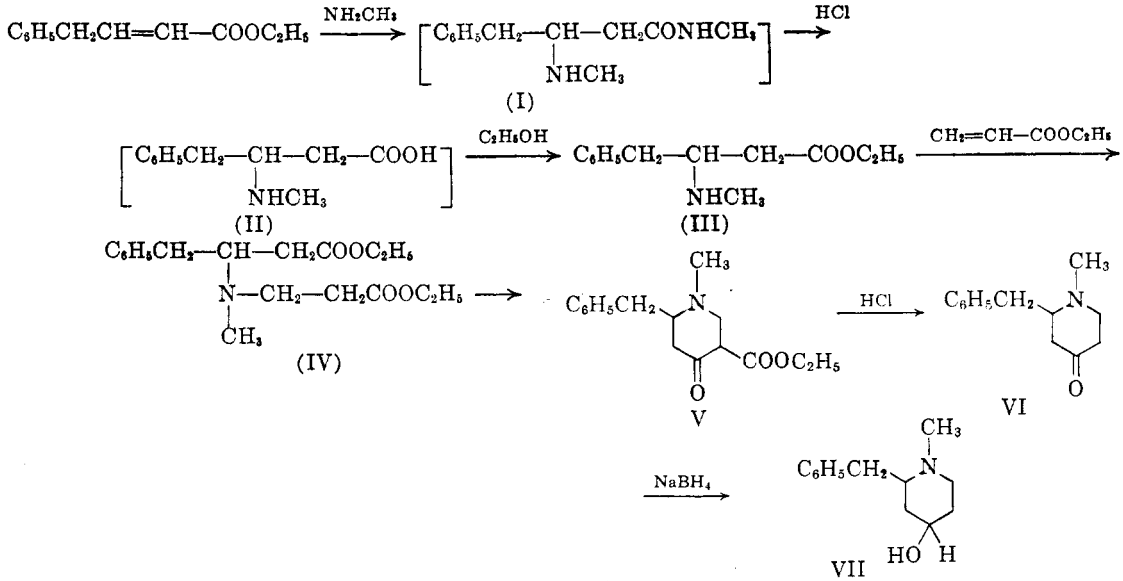
(1) Present address: Zambon S.p.A., Milano-Bresso, Italy.

(2) H. Moureau, P. Chovin, and L. Petit, *Bull. soc. chim. France*, 203 (1951).

(3) K. Morsch, *Monatsch. Chem.*, **60**, 50 (1932).

4-phenylbutyrate (III). It was found convenient to prepare III directly from ethyl 4-phenyl-2-butenoate without isolation of the intermediates. The total yield ranged between 47 and 50%. From III, ethyl 3-[*N*-(β-carbethoxyethyl)-*N*-(methyl)-amino]-4-phenylbutyrate (IV) was prepared by reaction with ethyl acrylate in ethanol, according to the process described for preparing di(β-carbethoxyethyl)methylamine[4]; yield 71%.

By ring closure of IV with sodium hydride in thiophene free benzene following the method of McElvain[5] for 1-benzoyl-3-carbethoxy-4-piperidone, crude 1-methyl-2-benzyl-5-carbethoxy-4-piperidone (V) was obtained in 91% yield and was subsequently purified through the hydrochloride. The crude product was submitted to acid hydrolysis and decarboxylated to 1-methyl-2-benzyl-4-piperidone (VI). This gave VII by reduction with sodium borohydride.



Experimental

Ethyl 3-Methylamino-4-phenylbutyrate (III) (Without Isolation of I and II).—To a solution of 130 g. of methylamine in 1500 ml. of absolute ethanol 36.7 g. of ethyl 4-phenyl-2-butenoate was added and the mixture allowed to stand 5 days. Then the mixture was evaporated to dryness *in vacuo* and the residue (38.2 g.) was taken up with ice water and made acidic with 10% hydrochloric acid (about 35 ml.). The insoluble portion was extracted with ethyl ether and the water layer was cooled, made alkaline with 50% potassium hydroxide, and saturated with potassium carbonate. The solution was extracted with ethyl methyl ketone and dried first over sodium sulfate, then over potassium carbonate. To the residue (A, 24.8 g.) 200 ml. of 1:1 hydrochloric acid was added, the solution refluxed for 6 hr. and then evaporated to dryness. The residue was dried by treatment with ethanol and benzene: the isolated solid weighed 35 g. (B). This solid was refluxed 6 hr. with 300 ml. of ethanol and 3 ml. of concd. hydrochloric acid, the mixture evaporated, and the residue made alkaline with potassium carbonate and extracted with ethyl ether. The extract was dried over potassium carbonate and evaporated. The residue was distilled *in vacuo;* yield 20 g., b.p. 130–135°/0.2 mm.

Anal. Calcd. for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.32. Found: C, 70.92; H, 8.58; N, 6.25.

The hydrochloride melted at 111–112°. *Anal.* Calcd. Cl, 13.80. Found: 13.78.

***N*-Methyl-3-methylamino-4-phenylbutyramide (I).**—Prepared as described above for III to the point where residue A was obtained; 1.2 g. of A was treated with oxalic acid in anhydrous ethyl ether. A crystalline precipitate was collected and recrystallized from ethanol; yield 0.9 g., m.p 114–115°.

Anal. Calcd. for $C_{12}H_{18}N_2O$: C, 69.86; H, 8.79; N, 13.57. Found: C, 70.12; H, 8.70; N, 13.81.

The hydrochloride had m.p. 155–156°.

3-Methylamino-4-phenylbutyric Acid (II).—One gram of crude *N*-methyl-3-methylamino-4-phenylbutyramide was heated over a water bath for about 3 hr. with 3–4 ml. of water, while continuously replacing the evaporating water, until ammonia evolution subsided. The solution was then evaporated to dryness and taken up with acetone. A crystalline product was collected and recrystallized from water. Yield 0.7 g., m.p. 218–219°.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.36; H, 7.82; N, 7.24. Found: C, 68.60; H, 7.55; N, 7.49.

Ethyl 3-[*N*-(β-carbethoxyethyl)-*N*-(methyl)amino]-4-phenylbutyrate (IV).—In a flask provided with a calcium chloride trap for moisture 12.5 g. of ethyl 3-methylamino-4-phenylbutyrate and 36 ml. of ethanol were charged. The mixture was cooled on ice and 7.5 ml. of ethyl acrylate was added portionwise in 10 min. The flask was kept 7 days at room temperature and the ethanol then removed by distillation. The residue was distilled *in vacuo;* yield 13 g., b.p. 160–165°/3–4 mm.

Anal. Calcd. for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.46; N, 4.35. Found: C, 67.84; H, 8.40; N, 4.41. The monooxalate had m.p. 130–131°.

1-Methyl-2-benzyl-5-carbethoxy-4-piperidone (V).—Six grams of sodium hydride was suspended in 160 ml. of anhydrous benzene in a 500-ml. flask under a nitrogen stream. Forty grams of ethyl 3-[*N*-(β-carbethoxyethyl)-*N*-(methyl)amino]-4-phenylbutyrate was added in 10 min., followed by 0.33 ml. of anhydrous ethanol as catalyst. The mixture was refluxed 4 hr., cooled on ice, and 15 ml. of water

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(5) S. M. McElvain and R. McMahon, *J. Am. Chem. Soc.*, **71**, 901 (1949).

added. The mixture was stirred for 0.5 hr., allowed to stand 3 hr., and filtered. The precipitate was washed three to four times with water and the filtrate was evaporated to dryness *in vacuo*. Yield 34.8 g. of crude product, used as such for the subsequent step.

Anal. Calcd. for $C_{16}H_{21}NO_3$: C, 69.78; H, 7.68; N, 5.08. Found: C, 69.94; H, 7.65; N, 4.92. The product gave a positive reaction with ferric chloride.

The hydrochloride had m.p. 172–173°. *Anal.* Calcd. N, 4.49. Found: N, 4.48.

1-Methyl-2-benzyl-4-piperidone (VI).—A mixture of 30.8 g. of V and 125 ml. of 1:1 hydrochloric acid was refluxed 2.5 hr. to a negative ferric chloride reaction. The mixture was filtered hot with charcoal, and the filtrate was evaporated to dryness *in vacuo*. The residue was dissolved in water and the solution made alkaline with 50% potassium hydroxide, saturated with potassium carbonate and then extracted with ethyl ether. The extract was dried over sodium sulfate then over potassium carbonate and evaporated to dryness *in vacuo*. The residue was distilled *in vacuo;* yield 13 g., b.p. 135–140°/0.2–0.3 mm. The product, when exposed to air, turned brown-red very rapidly.

Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.42; N, 6.88. Found: C, 77.10; H, 8.30; N, 6.65.

1-Methyl-2-benzyl-4-piperidol (VII).—Two grams of VI was dissolved in 40 ml. of methanol and 2 ml. of water. The solution was cooled on ice and 0.375 g. of sodium borohydride was added in 15 min. The reaction was exothermic. The solution was allowed to stand 3 hr. at 25° and then methanol was removed by distillation. The residue was extracted with a large amount of ethyl ether and the extract was dried over potassium hydroxide and concentrated to a small volume. On cooling 1.4 g. of VII melting at 115–116° separated.

Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.05; H, 9.32; N, 6.81. Found: C, 76.28; H, 9.15; N, 6.92.

Condensed Cyclobutane Aromatic Compounds. XX. Photolysis of the Isomeric 3,3-Diphenyldiazoindanones

M. P. CAVA, D. G. MCCONNELL, K. MUTH, AND M. J. MITCHELL

Evans Chemical Laboratory, The Ohio State University, Columbus 10, Ohio

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The photolysis of α-diazoindanones has proven to be a method of general applicability in the synthesis of benzocyclobutene derivatives.[1,2] In an attempt to prepare 2,2-diphenylbenzocyclobutene-1-carboxylic acid (I) by this method, we have studied the photolysis of 3,3-diphenyl-1-diazo-2-indanone (II).[2] Ultraviolet irradiation of diazo ketone II was carried out in a two-phase solvent system of ether and aqueous sodium bicarbonate, using a Pyrex glass vessel; however, acidification of the aqueous phase gave, not the expected benzocyclobutene acid (I), but rather a lactone (IV) of the same composition, $C_{21}H_{16}O_2$. Similarly, photolysis of the isomeric diazo ketone (III) gave only lactone IV.

Hydrogenolysis of IV in ethanol with palladium-on-charcoal catalyst gave *o*-(diphenylmethyl)phenylacetic acid (V). The identity of this acid was confirmed by an independent synthesis, starting from α,α-diphenyl-*o*-toluic acid (VI),[3] and proceeding *via* the acid chloride (VII) and the diazo ketone (VIII) to acid V.

In the formation of lactone IV, it seems likely that the initial process is a ring contraction of the diazo ketone (II or III) to give the benzocyclobutene acid (I). The acid, in the form of its sodium salt (Ia), might reasonably be expected to undergo cleavage of the four-membered ring to give an intermediate (IX) of the *o*-quinodimethane type, since such cleavage would be greatly facilitated by the resulting conjugation of the carboxyl and the phenyl substituents with the quinodimethane system.[4] Re-aromatization of the six-membered ring could then be accomplished by a simple 1,4-addition of water to IX, which would result in the formation of the sodium salt (X) of a hydroxy acid. Finally, acidification would cause ring closure to give the observed lactone IV. These proposals are supported by the fact that lactone IV, once it is formed, is not saponified by (nor is it soluble in) aqueous sodium bicarbonate solution. Hence, the material which is found dissolved in the bicarbonate phase of the reaction mixture and which gives the lactone on acidification, must be the sodium salt of the benzocyclobutene acid (Ia) or, what is more likely, of the hydroxy acid (X).

In preparing diazo ketone II, only a few modifications were made in the sequence of reactions reported in the literature.[5] Thus, 3,3-diphenyl-2-oximino-1-indanone was prepared from 3,3-diphenyl-1-indanone[6] by treatment with *n*-butyl nitrite and potassium *t*-butoxide in *t*-butyl alcohol in yields (80–85%) which are superior to those (40–50%) obtained by the literature method (*n*-butyl nitrite and sodium ethoxide in ethanol).[7] Diazo ketone II was found to be more easily purified by chromatography on Woelm Grade II neutral alumina with 1:1 methylene chloride–petroleum ether than by recrystallization from cyclohexane as described previously.[2]

Experimental[8]

3,3-Diphenyl-2-oximino-1-indanone.—3,3-Diphenyl-1-indanone[6] (25.0 g., 0.088 mole) was added with stirring and under nitrogen to a solution of potassium *t*-butoxide in *t*-butyl alcohol [prepared from 7.4 g. (0.189 mole) of potassium and 320 ml. of *t*-butyl alcohol]. When the indanone had

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(3) R. Brisson, *Ann. chim.*, [12] **7**, 311 (1952).

(4) A precedent for this proposal is found in the chemistry of 1,2-diphenylbenzocyclobutene: The compound readily undergoes ring cleavage under mild conditions to give the highly reactive species, α,α′-diphenyl-*o*-quinodimethane. *Cf.* F. R. Jensen and W. E. Coleman, *J. Am. Chem. Soc.*, **80**, 6149 (1958); M. P. Cava, M. J. Mitchell, and A. A. Deana, *J. Org. Chem.*, **25**, 1481 (1960).

(5) For a description of the latter stages of the sequence, see ref. 2.